REMARKS

Claims 1-25 were pending in the application. Claims 26-29 are added by the present amendment. Claims 1-25, and new claims 26-29 are under consideration. All of the pending claims have been rejected in an Office Action mailed March 22, 2002 (Paper 2).

The "Cross-reference to Related Applications" has been amended per the instructions of the Patent Office. Claims 11, 12 and 19 have been amended to recite "murine L-cell virus." Support for this amendment is found at page 22, lines 12-14 of the specification. Claims 24 and 25 have been amended to recite a "pleiomorphic cell that is not a transgenic cell, and is derived from a eukaryotic cell, containing at least one gene evolved from the genome of said eukaryotic cell." Support for the term"pleiomorphic cell" is found inherently throughout the specification, and specifically at page 7, lines 4-5 and page 29, lines 10-22. Support for the term "[a cell] that is not a transgenic cell" is inherent in the entire disclosure of the specification, and the claims as originally filed. Specific passages showing that the cells of the present invention are not transgenic are found at page 9, lines 5-23, page 15, lines 20-23, page 26, lines 16-18 and page 34, lines 11-19. The term "and is derived from a eukaryotic cell" finds support in the same points of the specification. The term "containing at least one gene evolved from the genome of said eukaryotic cell" finds support at page 15, lines 20-23, 26, lines 16-18, page 34, lines 3-19, and inherently in the entire disclosure of the specification. New claims 26-29 find support throughout the specification, and in claims 24 and 25 as originally filed. New claims 26-29 find further support at page 29, lines 17-22, of the specification. No new matter is introduced by the present amendments.

The Commissioner is hereby authorized to charge any necessary additional claim fees, or credit any overcharge, to deposit account number 02-2135, in the name of Rothwell, Figg, Ernst and Manbeck.

I. Double-Patenting Rejection

Applicant acknowledges the provisional rejection under the judicially-created doctrine of obviousness-type double-patenting. As the present claims have not yet been allowed, action on this rejection is premature. Should this become an actual rejection, applicant will at that time address the issue of a terminal disclaimer, and requests that the rejection be held in abeyance in the meantime.

II. Rejection Under § 101

The Patent Office has rejected claims 1-25 under 35 U.S.C. § 101 "because the claimed invention is not supported by either a credible asserted utility or a well-established utility, as the disclosed invention is inoperative." The Patent Office also asserts that the claims call for the "spontaneous generation" of bacteria. Office Action at 4. This last is not a correct interpretation of the invention, and naturally leads to an impression of incredulity since spontaneous generation (in the classic sense of producing life from inanimate or dead material) is indeed a long-discounted scientific theory. The assertion that the claims call for spontaneous generation of bacteria is simply untrue. Read in light of the specification, the claims clearly refer to methods of making ("producing") bacteria out of virally infected eukaryotic cells. This is not spontaneous generation; "de novo speciation" does not mean "the creation of life," as

the Patent Office asserts (Office Action at 4), but rather the evolution or changing of a species in to a distinguishable new species. Nothing is created, only changed in form. The assertion by the Patent Office that "the only recognized process in the art for the acquisition of new traits is mutation is well settled" is beside the point, as the data presented in the present specification (data that has been independently corroborated, as shown below), clearly demonstrates that in fact, accepted wisdom notwithstanding, there are ways other than mutation by which organisms can acquire new traits.[1] The data speaks for itself.

Accompanying this Response are two Declarations under 37 C.F.R. § 1.132 filed in the parent case, Serial No. 08/719,367, one by the inventor, Dr. Douglas Robinson, Ph.D., and one by an independent scientist, Dr. Anton Steuer, Ph.D., who conducted a rigorous confirmation of the experiments reported in the present application. Both of these Declarations present independent corroboration of the utility of the claimed methods.

The Robinson Declaration presents a "Final Report" prepared by Microbiological Associates, Rockville, Maryland (hereinafter "MA") at the request of Dr. Robinson. The experiments requested by Dr. Robinson were for the purpose of reproducing the process described in the present application. Robinson Declaration, paragraphs 4-5; Steuer Declaration, paragraph 3. The Steuer Declaration presents additional detail

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[1] Furthermore, microorganisms, such as bacteria and fungi, are known in the art to undergo very rapid and sometimes dramatic change in their morphological and physiological characteristics, a process that in nature does not take "millions of years" as the Patent Office asserts (in any event, the Patent Office is referring in this comment to evolution of prokaryotes to multi-cellular eukaryotes, which is not what occurs with the present methods). Office Action at 4.

regarding the work performed at MA. Dr. Steuer is the scientist who supervised the experiments by MA that corroborated the enabling quality of the disclosure and the utility of the invention, and is an expert in the field of cell culturing techniques. Dr. Steuer also is one of the scientists employed by Microbiological Associates who signed the Final Report. Robinson Declaration, Paragraph 5; Steuer Declaration, paragraph 2. The "Final Report" states in its Conclusion that

> "Two runs involving the periodic reintroduction of an aerobic atmosphere during an anaerobic eukaryotic cell culture phase resulted in the isolation of bacteria, specifically *Bacillus licheniformis*. . . . The isolation of bacteria from eukaryotic cells subjected to alternating anaerobic/aerobic cell culture conditions provides supporting evidence for the hypothesis of *de novo* evolution of bacteria from eukaryotic cells. On the other hand, the possibility of environmental contamination as the source of the bacterial isolates cannot be absolutely eliminated. Environmental contamination is unlikely due to the cGMP compliance procedures and practices employed in the performance of the sterility assays, which includes a stringent environmental and personnel monitoring program. Also, no tube, plate, or bottle inoculated with eukaryotic cell control samples or media control samples showed any microbial outgrowth. These negative results for all the numerous control samples tested minimized significantly the possibility of environmental contamination."
>
> (emphasis added)

The work reported in the Final Report was carried out under tightly-controlled sterility conditions and GMP. The results showed that neither the eukaryotic cell cultures used, nor the media, nor the equipment, showed any detectable microbial contamination -- in other words, there were no bacteria in any of the starting materials used, and none were introduced during the experiments. The Final Report also shows conclusively that microorganisms having all of the morphological characteristics of bacteria were isolated from the culture at the end of each of four experimental runs.

Dr. Steuer's Declaration explains the rigorous standards employed during the testing procedure to ensure that the starting material was not contaminated and that contamination did not arise during the course of the cell culturing procedures. Steuer Declaration, paragraphs 3-4 & 6. The equipment and procedures used at MA for this work met or exceeded the most rigorous standards present in the industry (Steuer Declaration, paragraph 6), and complied with, among others, the U.S. FDA Good Laboratory Practice Regulations, the U.S. E.P.A. GLP's, the United Kingdom CLP Compliance Programme, and the Japanese GLP Standard. Steuer Declaration, paragraph 7.

Dr. Steuer explains why, in his professional opinion, the production of bacteria was not due to "contamination." Steuer Declaration, paragraphs 8-10. In Dr. Steuer's opinion, the Patent Office had "applied a requirement of 'proving' a lack of contamination that is not applied by persons skilled in this field." Steuer Declaration, paragraph 8. It is Dr. Steuer's professional opinion that "any scientific inquiry wherein one must 'rule out' contamination, as set forth in the Office Action[2], is meaningless." Steuer Declaration, paragraph 8. As set forth in the Steuer Declaration, the claimed process was shown to produce bacteria upon anaerobic/aerobic culturing of virally-infected eukaryotic cells. Moreover, the report contains a Quality Assurance statement showing that FDA and EPA Good Laboratory Practices were followed. The report concludes that "[e]nvironmental contamination is unlikely," thus overcoming the Patent Office's position that the results were attributable to contamination.

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[2]Referring to the Office Action in the parent case, Serial No. 08/719,367.

Taken together, these Declarations establish the utility of the claimed methods, by demonstrating that they are, in fact, operative by any standard applied by persons of ordinary skill in the art. In view of this evidence, the rejection under § 101 should be withdrawn.

III. Rejections Under § 112, First Paragraph

The Patent Office has also rejected claims 1-25 under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Office Action states that "[i]t's unclear if the written description is sufficiently repeatable to avoid the need for a deposit." Passing on the fact that this statement concedes the operability of the methods and thus is inconsistent with the previous utility rejection, deposits were made of the bacteria produced by the claimed methods, and these deposits were in accordance with the Budapest Treaty, as expressly stated on page 8, lines 10-13 of the specification. As none of the claims recite specific bacterial isolates, amendment of the claims to recite specific ATCC accession numbers is neither necessary nor appropriate. The specification further states at page 9, lines 26-28 that suitable starting materials are publicly available, and also provides at page 9, line 29 to page 10, line 2, reference to techniques which can be used to produce additional starting cell cultures. Finally, the specification specifically discloses the public availability of all of the eukaryotic cells lines used as starting materials in the Examples, as follows:

Cell line	Availability	Citation to Specification
RT-HCMV	ATCC CRL 11655	page 22, lines 20-22
procine cerebral microvascular endothelial	Robinson, et al.	page 27, lines17-19
L929	ATCC CCL 1	page 27, lines 19-20
murine lymphoma	ATCC TIB52	page 27, lines 20-21
SV-40 transformed human colon	ATCC CRL 1807	page 28, lines 5-6
human colon adenocarcinoma	ATCC HTB 38	page 28, lines 6-7

The foregoing, together with the Declaration evidence presented herewith, conclusively shows the enabling nature of the specification, and the repeatability of the methods.

The Patent Office further bases its rejection of claims 1-25 on the assertion that the specification "does not reasonably provide enablement for methods for **producing** a bacterium that contains a eukaryotic and/or viral gene comprising culturing virally-infected eukaryotic cells under low oxygen conditions." Office Action at 6-7 (emphasis original). This assertion is directly contrary to the disclosure of the specification, which shows the production of a variety of bacteria from six different eukaryotic cell lines. By definition, this disclosure enables the claims because it teaches (indeed, demonstrates) how to employ the claimed methods to produce a bacterium. "The enablement requirement is met if the description enables any mode of making and using the claimed invention." Engel Industries, Inc. v. Lockformer Co., 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991).

The Patent Office states that "it does not appear that the claimed method would be suitable for the recovery of any and all bacteria." Office Action at 7. The applicant respectfully submits that the Patent Office has applied the wrong standard for enablement in this rejection. The claims on their face recite methods for producing "a bacterium." Thus, in order to meed the enablement requirements of § 112, first paragraph, the specification need only teach a person of ordinary skill in the art how to produce "a bacterium" (Engel Industries, supra), which it clearly does. In fact, the Robinson and Steuer Declarations confirm and conclusively establish that the methods disclosed in the specification enable the production of a number of different kinds of bacteria. The claimed methods need not lend themselves to producing "any and all" bacteria (this is a limitation inserted by the Patent Office that does not appear in the claims); the claims do not recite methods for producing specific bacteria, or all bacteria, just a bacterium, any bacterium, generally. In re Angstadt & Griffin, 190 U.S.P.Q. 214, 218 (Applicants are not required to disclose every species of their invention, even in an unpredictable art.) The statement that "the claims lack specific method steps for the recovery of the bacteria" is irrelevant -- the method does not necessarily require the isolation of the bacteria, and the Patent Office has provided no reason why such a step is required for enablement.

Additionally, the Office Action makes clear that the Patent Office has fundamentally misconstrued the nature of the invention in making this rejection. At page 7, the Patent Office states that "one of ordinary skill in the art would not reasonably expect any and all possible viral infected eukaryotic cultures to harbor or be contaminated by bacteria." Similar statements throughout the Office Action make clear that the Patent Office is

assuming that the products of the claimed methods are the result of bacterial contamination of the treated eukaryotic cultures. The Patent Office further states that "it is unclear what precautions were taken in the instant case to assure that the bacteria harvested are not incidental contaminants inadvertently introduced into the cell culture." Office Action at 7. The specification clearly states that the methods result in the acquisition by eukaryotic cells of all of the morphological characteristics of prokaryotes, and that the production of bacteria is *not* due to the presence of bacteria in the eukaryotic cell cultures. See, e.g., Comparative Examples 1/A, 1/B, 1/C, D (specifically page 26, lines 13-18), and 2/A. The Examples all provide considerable detail regarding both precautions taken against incidental contamination, and controls to monitor whether contamination had in fact occurred -- the results all indicated that there was no contamination. Indeed, in other portions of the Office Action the Patent Office acknowledges that this is the case. See, e.g., Office Action at 2, lines 23-26 ("methods of producing (isolating) bacteria from retrovirally transformed human endothelial cells"); at 3, lines 17-20 ("neither the bacterium nor the bacterial genome is introduced"). The Declarations provided herewith further confirm the accuracy of the specification on this point. Dr. Seuer in particular states that in his expert opinion, the position that the Patent Office took in the parent case, which is essentially the same as that taken in the present Office Action, "is not applied by persons skilled in the art," and such an inquiry is "meaningless" in the context of this invention. Seuer Declaration, paragraph 8. The assumption of the Patent Office underlying this rejection therefore is incorrect.

The Patent Office further states that the claimed method is unpredictable, and that it is not clear what steps actually produce the bacterium. Office Action at 8-9. The

Declarations accompanying this response conclusively demonstrate that the claimed methods are indeed completely repeatable. It also is of no significance that the precise step in which the bacteria are produced is not identified or defined -- an inventor does not need to show, or even understand, how his invention works, only that it does work. In Newman v. Quigg, the Federal Circuit stated that:

> "While it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works . . . neither is the patent applicant relieved of the requirement of teaching how to achieve the claimed result, even if the theory of operation is not correctly explained, or even understood."

11 U.SP.Q. 1340, 1345 (Fed. Cir. 1989). See also Fromson v. Advance Offset Plate, Inc., 219 U.S.P.Q. 1137, 1149 (Fed. Cir. 1983) ("it is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests."). The disclosure of the specification, as confirmed by the experiments discussed in the Robinson and Seuer Declarations, leave no doubt that the methods do indeed work. This is all that is required under § 112.

Finally, the Patent Office asserts that it is unclear how one of skill in the art would determine and assure that the actual viral and/or eukaryotic genes are indeed intact genes picked up, rather than random fragments thereof, or how one would determine if the genes were integrated into the genome. Office Action at 9. These assertions again assume that the bacteria produced by the claimed methods are contaminants, which, as discussed above, they are not. The issues raised by the Patent Office with regard to the genes themselves are not material to the claims. Whether or not the genes (which

term by definition means an intact coding sequence,[3] and is specifically defined as such at page 7, lines 8-12 of the specification), are intact is not pertinent given the accepted definition of a "gene," as is the issue of genomic integration, since the bacteria are formed from the eukaryotic cells. A person of ordinary skill in the art would recognize that any eukaryotic genes present in bacteria produced by the claimed methods would be intact, stable and integrated in the genome, because that would be their condition prior to performance of the claimed methods. In any event, methods for detecting, analyzing, evaluating and characterizing genes are routine procedures for the person of ordinary skill in the art.[4]

In view of the foregoing discussion, and the Declarations of Drs. Robinson and Steuer, applicant submits that the claims meet all of the requirements of the first paragraph of § 112, and requests that this rejection be reconsidered and withdrawn.

IV. Rejections Under § 112, Second Paragraph

The Patent Office has rejected claims 1-25 for failing to particularly point out and distinctly claim the subject matter which the applicant regards as his invention. Office Action at 9.

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[3]See, Lewin, B., Genes V, page 1242, Oxford University Press (1994), a copy of which is annexed for the Examiner's convenience.

[4]See, e.g., Sambrook, J., et al., Molecular Cloning, A Laboratory Manual, 2d ed., Chapter 9, Cold Spring Harbor Laboratory Press (1989). A copy of the table of contents for Chapter 9, which provides an outline of analytical techniques then available, is annexed hereto for reference, the entire chapter being rather voluminous and not strictly necessary to support Applicant's arguments. Applicant can provide the entire chapter if the Examiner so requires.

The Patent Office has found that claims 1 and 15 are rendered vague and indefinite by use of the term "producing," according to the Patent Office it is unclear whether "production" occurs, and further because it cannot be assessed whether any DNA picked up would necessarily constitute a gene. Applicant traverses this rejection. The first sentence of the second paragraph of 35 U.S.C. § 112 requires only that claims set out and circumscribe a particular area with a reasonable degree of precision and particularity. In re Miller, 169 U.S.P.Q. 597 (C.C.P.A., 1971); see also Hybritech v. Monoclonal Antibodies, Inc., 231 U.S.P.Q. 81 (Fed. Cir. 1986) (The claims need only "reasonably apprise those skilled in the art" as to their scope and be "as precise as the subject matter permits.") If a person of ordinary skill in the art would understand what s claimed, the second paragraph of §112 is satisfied. Seattle Box Co., Inc. v. Industrial Crating and Packing, Inc., 221 U.S.P.Q. 568, 574 (Fed. Cir. 1984). "Mathematical precision should not be imposed for its own sake; a patentee has the right to claim the invention in terms that would be understood by persons of skill in the field of the invention." Modine Mfg. Co. v. ITC, 37 U.S.P.Q.2d 1609, 1617 (Fed. Cir. 1996). See Shatterproof Glass Corp. v. Libby-Owens Ford, Co., 225 U.S.P.Q. 634, 641 (Fed. Cir. 1985) ("if the language is as precise as the subject matter permits, the courts can demand no more"). In the present case, the term "production" is as precise a term as the subject matter permits -- starting materials are treated in accordance with the claimed methods, and a bacterium containing a eukaryotic and/or viral gene results. This process can reasonably only be described as "production," and the term would be readily understood by persons of skill in the field of the invention. The second paragraph of § 112 is therefore satisfied.

The Patent Office further has found that claims 1 and 15 are rendered vague and indefinite by the use of the term "under low oxygen conditions." Applicant traverses this rejection, because this term is expressly defined in the specification at page 9, lines 15-18:

> "Preferably, the low oxygen conditions comprise alternating anaerobic culturing conditions with at least one brief period of exposure to an aerobic or microaerophilic condition."

The terms "anaerobic" and "aerobic" are defined in the specification at page 11, line 28 to page 12, line 5. Furthermore, the term "low oxygen conditions" does not even appear in claim 15. The term constitutes as precise a wording as the subject matter permits (Shatterproof Glass Corp., 225 U.S.P.Q. at 641), and would be understood by persons of ordinary skill in the art (Seattle Box Co., Inc., 221 U.S.P.Q. 574). The first paragraph of § 112 is therefore satisfied. In re Miller, 169 U.S.P.Q. 597 (C.C.P.A., 1971).

The Patent Office has found claims 2, 3, and 15 vague and confusing because they recite "subjecting the cells to an aerobic culturing step," while the claims from which they depend require culturing under "low oxygen conditions." First, claim 15 is an independent claim, and so this rejection can not properly apply to it. Furthermore, the claim element in question is actually "wherein said low oxygen conditions comprise anaerobic culture conditions with at least one exposure of the cells to aerobic or microaerophilic culture conditions." As stated above, "low oxygen conditions" are expressly defined at page 9, lines 15-18 of the specification to comprise alternating anaerobic and aerobic phases. Therefore claims 2 and 3, read in their entireties, are not vague or confusing, and the rejection warranted.

The Patent Office has found that the term "L-cell virus" appearing in claims 11-12 and 19 lacks sufficient antecedent basis, because "the independent claims lack a full spelling of the complete virus name" and "it does not appear to be a term of art." The term "L-cell virus" is indeed a term of art. Submitted along with this response is a screen print of the results of a search on the National Library of Medicine's "Gateway" database (found at http://www.nlm.nih.gov/libserv.html) showing that the search term "L-cell virus" produced 2729 hits that were journal citations. Also accompanying this response are the MEDLINE abstracts of two representative journal articles pre-dating the priority date of the present application (Radaelli, et al., *J. Gen Virol.*, 1984, 65:295-307, PubMed ID 6198451, and Robinson, et al., *Blood*, 1991, 77:294-305, PubMed ID 1985696) that show the use of the term "L-cell virus." The NLM "Gateway" search results and these two journal abstracts, demonstrate that "L-cell virus" is a term that was used and would have been understood in the art to mean a specific virus. In order to further clarify the term, claims 11, 12 and 19 also have been amended to read "murine L-cell virus." The second paragraph of § 112 is therefore satisfied.

The Patent Office has found claims 2 and 15 vague and indefinite in the use of the language "micoraerophilic conditions." This is a term of art. Submitted along with this response is a screen print of the results of a search on the National Library of Medicine's "Gateway" database showing that the search term "microaerophilic" produced 567 hits that were journal citations. Also accompanying this response is the MEDLINE abstract of a representative journal article pre-dating the priority date of the present application (Smith and Edwards, *J. Antimicrob Chemother*, 1995, 36:453-61, PubMed ID 8830009) that shows the use of the term microaerophilia/microaerophiles.

Inherent in the use of these terms is the term "microaerophilic" to describe the conditions under which the former exist. The NLM "Gateway" search results and this journal abstract demonstrate that "microaerophilic" is a term that was used, and would have been understood, in the art.

The Patent Office has deemed claims 1-24 incomplete because they lack a recovery step for the microorganisms obtained. Applicant traverses this rejection, because the claimed methods do not require isolation of the bacterium produced (applicant assumes this is the meaning of the term "recovery" intended by the Patent Office). The claimed methods are for the production of a bacterium, not the production of an isolated bacterium. The claims are operative because they recite method steps that result in the production of a bacterium -- what is done with the bacterium once it is produced (e.g., isolated for further characterization, used to make a vaccine, used to produce a particular protein product) is up to the person practicing the invention. Recovery of the bacterium from the culture medium is not required for the practice of the method, nor is it in fact required for the use of the product of the method, as there are any number of uses to which the bacterium product can be put that do not require that it be isolated. This rejection therefore is not warranted.

In view of the foregoing, applicant respectfully submits that the rejection of claims 1-25 under § 112, second paragraph, is not warranted, and requests that this rejection be reconsidered and withdrawn.

V. Rejection under § 102(b)

The Patent Office has rejected claims 24 and 25 as anticipated by, or in the alternative as obvious over, Bujard et al. (U.S. Patent No. 4,868,111) or Sloma et al. (U.S. Patent No. 4,695,543). The Patent Office asserts that these product-by-process claims are anticipated by the disclosure in these references of bacteria containing eukaryotic genes. Anticipation under 35 U.S.C. § 102 requires the presence in a single prior art disclosure of each and every element of a claimed invention. Lewmar Marine, Inc. v. Barient, Inc., 3 U.S.P.Q.2d 1766, 1767 (Fed. Cir. 1987).

Claims 24 and 25 have been amended to more clearly define the subject matter of the invention. They now recite:

> "A pleiomorphic cell that is not a transgenic cell, and is derived from a eukaryotic cell, containing at least one gene evolved from the genome of said eukaryotic cell, prepared by a process according to [claim 1/15]."

This amendment to the claims is believed to show clearly that the cells derived from the methods of the present invention, the cells of claims 24 and 25, are not transgenic cells, and that they contain genes that evolved from the genome of the parent cell, as opposed to being introduced by standard molecular techniques. At page 34, lines 3-19, there is a detailed discussion of genetic analysis of cells of the present invention that were derived from human eukaryotic cells, showing that human eukaryote-derived Alu and LINES inter-repeat elements were found. This data, together with the detected presence of multiple human genes previously mapped to widely separated human chromosomes, shows that the genome of the cells obtained (not just a gene or genes) was derived from the human genome. Furthermore, specifying that the cell is a "pleiomorphic cell ... derived from a eukaryotic cell" distinguishes the cells of the

present invention from untreated (unevolved) eukaryotic cells. As amended, claims 24 and 25 thereof would not be anticipated by references such as Bujard or Sloma, which do not disclose each and every limitation of the claims. New claims 26-29 are likewise not anticipated, as they include all of the distinguishing characteristics of the claims from which they depend, and in the case of claims 28 and 29, are further distinguished by being directed to cells that do not have the morphological characteristics of either eukaryotes, or prokaryotes.

The rejection is presented in the alternative as a rejection under 103(a). As a first matter, the substance of the rejection does not support a prima facie case of obviousness, as there is no showing of any of the three necessary factors, motivation, teaching or suggestion of all the claim elements, and a reasonable expectation of success. And, in view of the amendments to the claims, none of the three elements can be established in the prior art.

In view of the foregoing, applicant respectfully submits that claims 24 and 25, as amended, and new claims 26-29, are neither anticipated by, nor obvious over, the prior art, and requests that the rejection be reconsidered and withdrawn.

CONCLUSION

In view of the foregoing remarks, and further in view of the Robinson and Steuer Declarations, applicant submits that the present claims meet all of the requirements of 35 U.S.C. §§ 101, 102(b) and 112, first and second paragraphs, and are in condition for allowance. Applicant earnestly solicits withdrawal of the pending rejections, and favorable action on the claims.

RESPECTFULLY SUBMITTED,					
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Attachments: Marked-Up Copies of Amendments
2149-107.AMD

Marked-Up Copy of the Amended Paragraph

This application is a continuation of Application Serial No. 09/382,816, filed August 25, 1999, abandoned, which is a continuation of Application Serial No. 08/719,367, now U.S. Patent No. 6,022,730, filed September 25, 1996, which ~~was~~ is a Continuation-In-Part of Application Serial No. 08/261,977, filed June 17, 1994, abandoned.

Marked-Up Copy of the Amended Claims

11. (amended) The method according to claim 1, wherein said virally-infected cell is infected with a virus selected from the group consisting of the murine L-cell virus, simian immunodeficiency virus (SIV), human immunodeficiency virus (HIV), Ableson murine leukemia virus and Moloney murine leukemia virus.

12. (amended) The method according to claim 11, wherein said virus is the murine L-cell virus.

19. (amended) The method according to claim 15, wherein said virally-infected eukaryotic cell is a human brain capillary endothelial cell infected with the murine L-cell virus.

24. (amended) A ~~bacteria containing a eukaryotic gene~~ pleiomorphic cell that is not a transgenic cell, and is derived from a eukaryotic cell, containing at least one gene evolved from the genome of said eukaryotic cell, prepared by a process according to claim 1.

25. (amended) A ~~bacteria containing a eukaryotic gene~~ pleiomorphic cell that is not a transgenic cell, and is derived from a eukaryotic cell, containing at least one gene

evolved from the genome of said eukaryotic cell, prepared by a process according to claim 15.

26. (new) A cell according to claim 24 that is a bacteria.

27. (new) A cell according to claim 24 that has morphology that is neither prokaryotic nor eukaryotic.

28. (new) A cell according to claim 25 that is a bacteria.

29. (new) A cell according to claim 25 that has morphology that is neither prokaryotic nor eukaryotic.